PATENT SPECIFICATION

Inventors: JOHN YATES and RAYMOND SPENCER AIRS

814,647

Date of filing Complete Specification: March 28, 1956.

Application Date: May 9, 1955. No. 13409/55.

Complete Specification Published: June 10, 1959.

Index at acceptance:—Class 2(3), C6, 17(A: C).

International Classification:—C07d, f.

COMPLETE SPECIFICATION

A process for the Manufacture of Organoboron Compounds

We, "SHELL" RESEARCH LIMITED, a British Company, of St. Helen's Court, Great St. Helen's, London, E.C.3, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention provides a novel process for the preparation of organo-boron compounds which comprises reacting an organo-alkali metal compound with a boron trihalide or a triester of boric acid in an anhydrous inert liquid reaction medium, with cooling if necessary, to produce the corresponding organo-boron halide or organoboric acid-ester complex.

In extensions of the above process, the organoboric acid ester complex is reacted with an anhydrous hydrogen halide to produce the organoboric acid ester, or the organoboron halide, organoboric acid ester complex or organoboric acid ester is reacted with water to produce the corresponding organoboric acid.

The organoboron compounds produced by the above processes have one or two organo groups attached to the boron atom, each by a carbon-to-boron linkage.

The organo-alkali metal compound used in the process of the invention is preferably a lithium, sodium or potassium compound, the organo group being attached to the metal by a carbon-to-metal linkage. The organo group may be an acyclic or cyclic hydrocarbon group which may be saturated or unsaturated. Preferably, the hydrocarbon group is an aromatic hydrocarbon group, for example, a phenyl group. The organo group may also be a heterocyclic group, for example, a furyl or thiophene group. The organo group may carry one or more substituent groups which are inert with respect to the alkali metal substituent, for example, hydrocarbon, nitro, etherified hydroxyl, and trifluoromethyl groups and the group OM where M represents an alkali metal.

Examples of organo-alkali metal compounds which may be used in the process of the invention are butyllithium, ethylsodium, alkali metal alkyne derivatives, benzylsodium, benzylpotassium, sodium triphenylmethyl, o-aminophenyllithium, p-nitrophenyllithium, dibenzofuryllithium and thioanisylphenyllithium. Phenyllithium and phenylsodium are particularly suitable compounds for use in the present process.

The organo-alkali metal compounds may be obtained by any process known in the art for preparing these compounds. A convenient method is to react a halohydrocarbon, preferably a chloro- or bromo-derivative, with two equivalent amounts of the alkali metal, preferably in finely divided state or in thin strips, in an indifferent solvent. In this method of preparation, the halohydrocarbon may also carry a substituent, for example, a hydroxyl group which will react with the alkali metal provided an additional proportion of alkali metal is used. Anhydrous ether, ligroin, toluene and xylene are suitable solvents for this purpose. The organo-alkali metal thereby produced may be used in the process of the invention without being isolated.

Organo-alkali metal compounds may also be prepared by reacting an alkylalkali metal, for example, butyllithium or amylsodium, with an aromatic hydrocarbon or a heterocyclic compound which may carry one or more substituents. With an etherified hydroxyl or trifluoromethyl substituent group, metallation occurs predominantly in the nucleus in the ortho-position to the substituent group. With a methyl mercapto group as a nuclear substituent, however, metallation occurs in the methyl portion of this group and not in the nucleus. Metallation also occurs in the methyl substituent groups of methylpyridines. The aromatic hydrocarbon or heterocyclic compound may also carry a nuclear halogen substituent, in which case metallation occurs in the position of this halogen substituent in the ring. The halogenated aromatic or heterocyclic compound may also carry a hydroxy

[Price 3s. 6d.]

Price 4s 6d.

substituent group, for example, p-bromophenol, provided an additional equivalent of alkylalkali metal is used to react with this group.

The organo-alkali metal compound is reacted in the process of the invention with a boron trihalide. Boron trichloride or boron trifluoride are preferred for this purpose as they are commercially available substances. They may be used either as such, or in the form of an addition compound with an ether, for example, with the ether used as the reaction medium. Alternatively, the organo-alkali metal compound is reacted with a triester of boric acid. This ester may be derived from an alcohol or from a phenol. Advantageously it is derived from an aliphatic alcohol containing from 1 to 5 carbon atoms in the molecule, particularly methyl alcohol, as such alcohols are readily separated in any subsequent hydrolysis of the organoboric acid ester to the organoboric acid.

The reaction between the organoalkali metal and the boron trihalide or boric acid triester may be effected in various ways. While it is theoretically possible to contact the liquid or vaporised boron compound with the solid organoalkali metal compound, for example, in finely divided form, it is unlikely that such a reaction could be performed in a controllable manner. It is therefore necessary to effect the reaction in a liquid medium, which may be a solvent for one or both reactants. The liquid medium employed should be one which remains liquid at the low temperature at which the reaction is generally effected and should, of course, be anhydrous. Suitable reaction media are, for example, diethyl ether, ligroin, toluene or commercial xylene. Where a volatile boron compound is used as the one reactant, the vapour may be passed gradually into the solution or suspension of the organoalkali metal in the inert liquid. It is, however, in general advantageous to dissolve the volatile reactant in an inert liquid and add the resulting solution gradually to the solution or suspension of the organoalkali metal in an inert liquid.

The temperature at which the reaction between the organoalkali metal and the boron trihalide or boric acid triester is effected depends to some extent on the nature of the boron-containing reactant and on the liquid reaction medium employed. In general, it is desirable to operate at temperatures below 0° C. if appreciable yields of the desired products are to be obtained. Thus when an ester of boric acid is used in an ethereal reaction medium, reaction temperatures of below −20° C and preferably of about −60°C. are desirable. When, however, a hydrocarbon is used as the reaction medium instead of an ether, reaction temperatures up to about +70°C. may be employed without appreciable reduction in yield. Reaction temperatures of −20° C and below, for example, −60°C. are also preferable when boron trihalides are used as reactants though temperatures up to about +12°C. can be used with boron trichloride. If desired, increased operating pressures may be employed, particularly when boron trifluoride is used.

The reaction between the organo-alkali metal and the boron trihalide or boric acid triester should be carried out in an anhydrous, inert liquid reaction medium, i.e., in the absence of any other substances which will react with one or both of these reactants, for example, hydroxylic compounds such as water or alcohols.

The organoboron halide, or organoboric acid ester or ester complex obtained as the reaction product of the process of the invention may be isolated by any suitable method. For example, the reaction mixture obtained when organo-alkali metal compounds are reacted with boron trihalides may be decanted and/or filtered, under anhydrous conditions where necessary, to remove precipitated byproducts such as alkali metal halides. The solvent and volatile impurities can then be removed by distillation and the residue purified by distillation, if necessary under reduced pressure, or by recrystallisation from a suitable solvent. This method is not in general suitable where a boric acid triester has been used as a reactant since the reaction product appears to be an ester complex probably of the type

$$Na^+[(PhB(OR)_3]^-$$

which may be soluble or insoluble in the reaction medium.

Organoboric acid ester complexes which are insoluble in the reaction medium may be isolated by filtering the reaction mixture and extracting the residual solid, comprising a mixture of the complex and alkali metal halide formed in the preparation of the organo-alkali metal compound, with isopropylamine to remove the complex. The ester complex can then be recovered from the resulting extract by evaporating the isopropylamine. Organoboric acid ester complexes which are soluble in the reaction medium are conveniently isolated by removing the volatile constituents of the reaction mixture, for example by distillation, if necessary under reduced pressure, and isolating the complex by means of isopropylamine as described above.

The organoboric acid ester may be obtained by reacting the organoboric acid ester complex with an anhydrous hydrogen halide, preferably hydrogen chloride. This is suitably effected by passing anhydrous hydrogen chloride into the reaction mixture in which the complex has been formed, though the isolated complex, preferably suspended in an inert reaction medium, may be used if desired. The organoboric acid ester can be isolated by removing the alkali metal halide and the reaction medium and may be purified if necessary,

as by distillation. Alternatively, and according to an extension of the process of the invention the organoboron halide, organoboric acid ester complex or organoboric acid ester may be hydrolysed to the corresponding organoboric acid by reaction with water. Where a triester of boric acid has been used as a reactant in the process of the invention, hydrolysis is preferably effected with an aqueous solution of a mineral acid to combine with the alkali formed. Suitably, the reaction mixture is agitated with a dilute aqueous mineral acid solution, the solvent layer containing the organoboric acid separated and the solvent and any low boiling impurities, such as lower aliphatic alcohols, removed by distillation. Steam distillation may be employed to remove higher boiling impurities, such as higher alcohols, when boric acid triesters of such alcohols have been used as reactants. The organoboric acid may be filtered off from the distillation residue or may be extracted from it by means of ether. Advantageously, the distillation residue is first made alkaline and then extracted with ether or other solvent to remove non-acidic impurities and the purified organoboric acid then liberated by acidifying the alkaline solution. The organoboric acid may be recrystallised from benzene, aqueous alcohol or other suitable solvent. Owing to the readiness with which organoboric acids lose water to form anhydrides, it is preferable to use water or an aqueous organic solvent such as aqueous alcohol for recrystallisation.

The organoboron compounds produced by the process of the invention are chiefly organoboronic compounds in which the boron atom is attached to one organic radical. Small quantities of organoborinic compounds in which the boron atom is attached to two organic radicals are sometimes formed simultaneously and may be separated from the boronic compounds by fractional distillation, crystallisation or other suitable means. The mixtures of organoboron acids containing one or two organic groups attached to the boron atom are conveniently separated by washing the mixture with light petroleum (for example, of 60—80°C. or 80—100°C. boiling range), in which the latter are more soluble. In some cases, it is possible to convert the borinic compound into the boronic compound. Thus, diphenylborinic acid may be converted into phenylboronic acid by treatment with a halogen such as chlorine or bromine in presence of water, or with hydrogen peroxide, according to the method of N. N. Mel'nikov given in Chemical Abstracts, 1936, Volume 30, page 5571.

The following examples illustrate the process of the invention, the parts by weight (p.b.w.) bearing the same relation to the parts by volume (p.b.v.) as the kilogram bears to the litre.

EXAMPLE I

Phenylboronic acid

A solution of phenyllithium was prepared from bromobenzene (78.5 p.b.w.; 0.5 mol.) and lithium strips (8.6 p.b.w.; 1.25 atoms) in dry ether (375 p.b.v.) under an atmosphere of nitrogen. The solution was decanted from excess lithium and added dropwise with stirring to a solution of tri-n-butyl borate (116 p.b.w.; 0.5 mol.) in dry ether (200 p.b.v.), the reaction temperature being maintained at between −60°C. and −65°C. by cooling in a mixture of isopropyl alcohol and solid carbon dioxide. The reaction mixture was allowed to warm to room temperature by standing overnight. The resulting solution was hydrolysed, by adding it dropwise to aqueous sulphuric acid (300 p.b.v.) containing 10 per cent by weight of H_2SO_4, which was stirred vigorously and cooled in an ice/salt bath.

The ether layer was separated and combined with the ether extracts obtained by extracting the aqueous layer twice using 100 p.b.v. of ether each time. The ether was removed by distillation, leaving a butanol solution which was made alkaline by adding potassium hydroxide (65 p.b.w. in water (350 p.b.v.). The butanol was removed by steam distillation under a pressure of 28 millimetres of mercury and the aqueous solution was filtered from a gummy residue (2.5 p.b.w.) and acidified with aqueous sulphuric acid containing 10% by weight of H_2SO_4. The acid solution was heated to boiling, filtered hot and the residue extracted with boiling water (2×10 p.b.v.).

The filtrates were combined and cooled and the precipitated solid was collected and crystallised from a mixture of benzene (150 p.b.v.) and light petroleum (b.p. 40—60°C.; 50 p.b.v.) as a white powder (26.4 p.b.w.; 0.22 mol.; 43% yield) m.p. 215—216°C. (with oil bath preheated to 200°C.). This was phenylboronic acid.

EXAMPLE II

Phenylboronic acid and diphenylborinic acid

A solution of phenyllithium prepared from bromobenzene (314 p.b.w.; 2.0 mol.) and lithium (30.8 p.b.w.; 4.4 atoms) in dry ether (1400 p.b.v.) was decanted from excess lithium and added dropwise to a stirred solution of trimethyl borate (208 p.b.w.; 2.0 mol.) in dry ether (400 p.b.v.), the reaction temperature being maintained below −65°C. by cooling in a mixture of isopropyl alcohol and solid carbon dioxide. The clear solution was allowed to warm to room temperature overnight. It was then added slowly to aqueous sulphuric acid (1200 p.b.v.) containing 10 per cent by weight of H_2SO_4, with stirring and cooling in ice.

The ethereal layer was separated and the

aqueous layer was extracted three times with ether, using 200 p.b.v. each time. The combined ether solutions were distilled to dryness from a boiling water bath and the off-white residue was recrystallised from water and then from a mixture of equal parts by volume of benzene and light petroleum (b.p. 40—60°C.) giving colourless needles of phenylboronic acid (20.5 p.b.w.; 0.17 mol.; 8.5% yield), m.p. and mixed m.p. 214—216°C.

The mother liquor was distilled to remove the solvent, a black oily residue being obtained. (This residue (86.6 p.b.w.) was distilled under reduced pressure and gave an initial fraction consisting of water (about 25 p.b.w.) and a fraction which distilled at 88°C. under a pressure of 1.0 millimetres of mercury and was proved to be diphenyl).

The distillation residue containing diphenylborinic acid was dissolved in aqueous ethanol solution containing 50 per cent by volume of ethanol and a solution of monoethanol-amine (15 p.b.v.) in 15 p.b.v. of the aqueous ethanol solution was added. The mixture, from which a precipitate began to separate, was stirred at room temperature for 30 minutes, cooled in ice and filtered. The residue was dissolved in benzene, reprecipitated by adding light petroleum (b.p. 70°—95°C.) and finally crystallised from aqueous ethanol containing 30 per cent by volume of ethanol. The product was dried at 60°C. under 15 millimetres pressure of mercury for 2 hours, giving 2-aminoethyl diphenylborinate (63 p.b.w.) as off-white platelets, m.p. 189°C. Analysis, found N, 6.3%: calculated for $C_{14}H_{16}ONB$, N, 6.2%.

Example III

Phenylboronic acid

Phenylsodium was prepared as described by Gilman and Jones (J.A.C.S., 1940, 62, 1514) from chlorobenzene (50.6 p.b.w., 0.45 mol.) and sodium (23 p.b.w.; 1.0 atom) in toluene (300 p.b.v.). The resulting mixture was stirred and cooled to −30°C. during the dropwise addition of a slurry of methyl borate (52 p.b.w.; 0.5 mol.) in benzene (250 p.b.v.) also cooled to −30°C. The mixture was stirred and allowed to warm to room temperature. After 3 hours, ethanol (250 p.b.v.) was added, followed by water (500 p.b.v.). The aqueous layer was separated and stripped under reduced pressure until the volume was about 300 p.b.v. The solution was made up to 500 p.b.v. with distilled water and acidified (to Congo red indicator) with concentrated hydrochloric acid. The mixture was heated to boiling and filtered from a dark brown oil. Extraction of the cooled filtrate 5 times with ether (50 p.b.v. each time) followed by evaporation of the combined extracts gave a light brown residue. This was crystallized from water (100 p.b.v.) using decolourising charcoal.

Phenylboronic acid (5.5 p.b.w.; 10% yield), was obtained, m.p. 215—216°C., when the melting point tube containing the acid was immersed in the bath preheated to 214°C.

Example IV

Phenylboronic acid

Sodium (27.3 p.b.w.; 1.19 mol.) was converted to a dispersion (particle size 10—25 microns) in dry toluene (96 p.b.w.) using 1% w/w oleic acid as dispersing agent. The mixture was cooled to 25—30°C. and chlorobenzene (58 p.b.w.; 0.52 mol.) in toluene (50 p.b.v.) was gradually added. The solution was then cooled to −60°C. and a solution of methyl borate (60 p.b.w.; 0.58 mole) in dry ether (180 p.b.v.) added with stirring. After warming to room temperature, residual sodium was destroyed by adding industrial methylated spirit (50 p.b.v.) at below 10°C. Hydrolysis was effected by adding 300 p.b.v. of 7% aqueous sulphuric acid solution and the ether layer separated. The aqueous solution was twice washed with 150 p.b.v. of ether and the combined ether/toluene solutions were distilled to remove ether and most of the toluene. Sodium hydroxide (30 p.b.w.) in water (150 p.b.v.) was added to the orange brown liquid residue and the mixture distilled to remove residual toluene. The mixture was cooled, extracted with ether to remove neutral products and acidified with hydrochloric acid. The mixture was extracted with ether (3 x 100 p.b.v.), the extract evaporated and the viscous brown residue washed with light petroleum to remove any diphenylborinic acid. A light brown powder (13.2 p.b.w.) remained, representing a yield of 21.5% on the chlorobenzene taken. Two recrystallisations from water gave a product m.p. 208—211°C.; acid value 461 milligrams of potassium hydroxide per gram (theory 460), boron content 8.8%, theory 8.9%.

Example V

Phenylboronic acid

Phenylsodium was prepared by reacting sodium (27.3 p.b.w.; 1.19 atoms) with chlorobenzene (58.0 p.b.w.; 0.52 mol.) as described in Example IV and was then added gradually to a stirred solution of boron trichloride (72 p.b.w.; 0.61 mol.) in dry toluene (60 p.b.v.) the temperature of the reaction mixture being kept below −20°C. After addition was complete, industrial methylated spirit (150 p.b.v.) was added to destroy excess sodium and boron trichloride, the temperature being kept below 15°C. The product was then hydrolysed by adding 300 p.b.v. of 20% sulphuric acid and the two layers formed were separated. The aqueous layer was twice washed with 150 p.b.v. of ether and the washings added to the organic layer. The combined layers were extracted 3 times with 50 p.b.v. of 20% sodium hydroxide solution. The combined alkaline extracts were acidified with sulphuric acid, extracted with ether (3 x 100 p.b.v.) and the extracts evaporated to give a yellow solid. Wash-

ing this yellow solid with light petroleum (2 × 50 p.b.v.) removed the colour to give phenylboronic acid as a white powder (6.7 p.b.w.; 10.9%) m.p. 204°—206°C.

A further quantity of material (3.3 p.b.w.; 5.4%) was isolated from the light petroleum after standing overnight.

Example VI

Phenylthiomethylboronic acid

$Ph.S.CH_2B(OH)_2$

Butyl lithium was prepared from butyl bromide (101.5 p.b.w.; 0.75 mol.) and lithium (10.5 p.b.w.; 1.5 atoms) in dry ether (500 p.b.v.) and methylphenyl sulphide (62 p.b.w.; 0.5 mol.) in dry ether (150 p.b.v.) was then added and the mixture refluxed for 15 hours. The mixture was then cooled to 0°C. and filtered through glass wool into a stirred solution of methyl borate (52 p.b.w.; 0.5 mol) in dry ether (150 p.b.v.) cooled to −40° to −50°C. After warming to room temperature, the mixture was acidified with 3N hydrochloric acid and the ether layer separated and washed four times with 3N sodium hydroxide solution, using 250 p.b.v. each time. The combined alkaline washings were acidified with concentrated hydrochloric acid. Extraction three times with ether (250 p.b.v. each time) and evaporation of the extract gave an orange oil, from which a white solid separated on cooling. This solid was filtered off and recrystallised from water giving white plates of phenylthiomethylboronic acid (11 p.b.w.) m.p. 110° C. It had an acid value of 328 milligrams of potassium hydroxide per gram; theoretical value 334.

Example VII

2:5-Dimethoxyphenylboronic acid

Hydroquinol dimethyl ether (69 p.b.w.) in anhydrous ether (500 p.b.v.) was metallated with butyl lithium (0.5 mol) in anhydrous ether (500 p.b.v.). After 60 hours at room temperature the reaction mixture was added to a solution of methyl borate (52 p.b.w.; 0.5 mol.) in anhydrous ether (400 p.b.v.) at −40° C. with stirring. After warming to room temperature the mixture was acidified with a mixture of concentrated hydrochloric acid (100 p.b.v.) and water (200 p.b.v.). The ether layer was separated and the aqueous layer was washed twice with 250 p.b.v. of ether. The combined ether solutions were extracted with a solution of potassium hydroxide (56 p.b.w.) in water (300 p.b.v.). Acidification of the aqueous extract with hydrochloric acid was followed by extraction three times with ether using 100 p.b.v. for each extraction. The residue obtained by evaporation of the ether was crystallised from boiling water giving white needles (8 p.b.w.) of 2:5 - dimethoxyphenylboronic acid, m.p. 95°—96°C. Found: C, 52.9%, H, 6.2%; $C_8H_{11}O_4B$ requires C, 52.8%, H, 6.1%. Acid value 308 milligrams of potassium hydroxide per gram; theoretical value 313.

An insoluble dark-red oil remained.

2:6 - Dimethoxyphenylboronic acid was prepared in a similar way from the dimethyl ether of resorcinol, 4 p.b.w. of white needles, m.p. 102°C. being obtained. Found: C, 51.8%, H, 6.2%; $C_8H_{11}O_4B$ requires C, 52.8%, H, 6.1%. A red insoluble oil was again obtained.

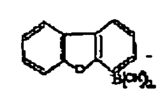
Example VIII

Benzfuryl-2-boronic acid

Butyl lithium was prepared from butyl bromide (101.5 p.b.w.; 0.75 mol.) and lithium (10.5 p.b.w.; 1.5 atoms) in dry ether (500 p.b.v.) and benzofuran (59 p.b.w.; 0.5 mol.) in dry ether (150 p.b.v.) was added dropwise. The mixture was refluxed for two hours and then added to a stirred solution of methyl borate (52 p.b.w.; 0.5 mol.) in dry ether (250 p.b.v.) cooled at −60°C. After warming to room temperature overnight, the mixture was hydrolysed with 3N sulphuric acid (300 p.b.v.). The ether layer was separated and washed three times with 3N sodium hydroxide solution using, respectively, 250, 150 and 100 p.b.v., and adding sufficient water each time to give two clear liquid phases. The combined alkaline solutions were acidified with concentrated hydrochloric acid and cooled to 0°C. when the separated oil solidified. The solid was filtered off (78 p.b.w.) and recrystallised from water twice, being obtained finally as colourless crystals (37.5 p.b.w.), m.p. 135°C. This was benzfuryl-2-boronic acid. It had an acid value of 343 milligrams of potassium hydroxide per gram; theoretical value 346.

Example IX

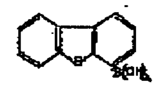
Dibenzfuryl-4-boronic acid



A solution of n-butyl lithium from n-butyl bromide (68.5 p.b.w.; 0.5 mol. and lithium (7.0 p.b.w.; 1.0 g. atom) in dry ether (250 p.b.v.) was added to a stirred solution of dibenzofuran (84 p.b.w.; 0.5 mol.) in dry ether (650 p.b.v.). The mixture was refluxed for four hours, cooled and filtered through glass-wool into a solution of methyl borate (52 p.b.w.; 0.5 mol.) in dry ether (250 p.b.v.); cooled in a mixture of solid carbon dioxide and light petroleum (b.p. 100—120°C.) at −65°C. The internal temperature was maintained below −30°C. When the addition was completed the mixture was stirred for 30 minutes, warmed to 0—5°C. and hydrolysed by the addition of concentrated sulphuric acid (50 p.b.v.) in water (1000 p.b.v.). The ether

layer was separated and the aqueous layer was twice washed with 250 p.b.v. of ether. The combined ether solutions were washed four times with 250 p.b.v. of a 2N solution of sodium hydroxide and the extracts were stirred and acidified to Congo red with concentrated hydrochloric acid. The solid which separated was collected and crystallised from benzene giving 24.5 p.b.w. of dibenzfuryl-boronic acid m.p. 255°C—258°C. It had an acid value of 266 milligrams of potassium hydroxide per gram; theoretical value 265. Unchanged dibenzofuran (8 p.b.w.) was obtained by evaporation of the alkali-insoluble ether fraction.

EXAMPLE X
Dibenzthienyl-3-boronic acid



Butyl lithium was prepared in anhydrous ethereal solution (300 p.b.v.) from lithium (8.6 p.b.w.; 1.25 g. atom) and n-butyl bromide (68.5 p.b.w.; 0.5 mol.). The solution was filtered through glass wool into a stirred solution of dibenzothiophene (92.0 p.b.w.; 0.5 mol.) in dry ether (1000 p.b.v.). The mixture was refluxed for 18 hours, cooled and added with stirring to a solution of methyl borate (52 p.b.w.; 0.5 mol.) in ether (100 p.b.v.) cooled to −60°C. The yellow mixture was allowed to warm to room temperature overnight and acidified with concentrated sulphuric acid (50 p.b.v.) in water (500 p.b.v.). The ether layer was separated and the aqueous solution was twice extracted with 250 p.b.v. of ether. The combined ethereal solutions were washed with water (200 p.b.v.) and extracted with 10% sodium hydroxide solution (4× 200 ml.). Acidification with concentrated hydrochloric acid gave a white precipitate which was collected and purified by dissolving in 10% sodium hydroxide solution at room temperature and reacidifying, three times. The final precipitate was filtered off, washed well with distilled water and dried under an infra red lamp. Dibenzthienyl-1-boronic acid was obtained as white product (4.5 p.b.w.) melting point above 360°C. It had an acid value of 248 milligrams of potassium hydroxide per gram; (theoretical value 246) with a tendency to sublime at 205°C./0.05 mm. Unchanged dibenzothiophene (67.7 p.b.w.) was recovered from the ether solution m.p. 97.5°C. after crystallisation from 90% aqueous isopropyl alcohol.

EXAMPLE XI
Thionaphthenyl-2-boronic acid

Thionaphthene was metallated with butyl lithium in dry ether. Reaction with methyl borate in ether at −40°C., followed by hydrolysis gave the thionaphthenyl-2-boronic acid, m.p. 259°—260°C. Found: S, 16.6%; $C_8H_7O_2SB$ requires S, 18.0%. Acid value 299 milligrams of potassium hydroxide per gram; theoretical value 315.

The organo boron compounds produced by the process of the invention have use as intermediates and lubricant additives. In particular, the organo boron acids and their salts and esters are active in controlling the growth of plants, particularly of dicotyledonous plants.

WHAT WE CLAIM IS:—

1. A process for preparing organoboron compounds which comprises reacting an organoalkali metal compound with a boron trihalide or with a triester of boric acid in an anhydrous, inert liquid reaction medium, with cooling if necessary, to produce the corresponding organoboron halide or organoboric acid ester complex.

2. A process as claimed in claim 1 wherein the organoalkali metal compound is an aromatic or heterocyclic lithium or sodium compound.

3. A process as claimed in claim 1 or 2 wherein a triester of boric acid is used in an ethereal reaction medium and the reaction temperature is maintained at below −20°C.

4. A process as claimed in claim 1 or 2 wherein a triester of boric acid is used in a hydrocarbon reaction medium and a reaction temperature up to about 70°C. is used.

5. A process as claimed in any one of the preceding claims wherein the triester of boric acid is derived from an alcohol containing from 1 to 5 carbon atoms in the molecule.

6. A process as claimed in claim 1 or 2 wherein boron trichloride is used as reactant.

7. A process as claimed in claim 1, 2, or 6 wherein the liquid reaction medium is diethyl ether, ligroin, toluene or commercial xylene.

8. An extension of the process claimed in any one of the preceding claims wherein the organoboric acid ester complex is converted to the organoboric acid ester by reaction with an anhydrous hydrogen halide.

9. An extension as claimed in claim 8 wherein anhydrous hydrogen chloride is used.

10. An extension as claimed in claim 8 or

9 wherein the anhydrous hydrogen halide is passed into the reaction mixture in which the organoboric acid ester complex has been formed.

11. An extension of the process claimed in any one of claims 1 to 7 wherein the organoboron halide or organoboric acid ester complex or organoboric acid ester is hydrolysed to the corresponding organoboronic or organoborinic acid.

12. A process for preparing organoboron compounds substantially as hereinbefore described with reference to the Examples.

13. Organoboron compounds whenever prepared by a process claimed in any one of the preceding claims.

H. I. DOWNES,
Agent for the Applicants,
St. Helen's Court, Great St. Helen's,
London, E.C.3.

PROVISIONAL SPECIFICATION

A process for the Manufacture of Organoboron Compounds

We, "SHELL" RESEARCH LIMITED, a British Company, of St. Helen's Court, Great St. Helen's, London, E.C.3, do hereby declare this invention to be described in the following statement:—

This invention provides a novel process for the preparation of organoboron compounds which comprises reacting, in the absence of a hydroxylic compound, an organo-alkali metal with a halide, ester or ester halide of boric acid to produce the corresponding organoboric acid derivative.

According to a further feature of the above process, the organoboric acid halide, ester or ester halide thereby produced is reacted with water to produce the corresponding organoboric acid.

According to a still further feature of the process of the invention, the organoboric acid halide or halide ester is reacted with an alcohol to produce an organoboric acid ester.

The organoboron compounds produced by the above processes have one or two organo groups attached to the boron atom, each by a carbon-to-boron linkage. The boron atom accordingly is attached respectively to two halogen atoms and/or ester groups or to two hydroxyl groups, or to one of said atoms or groups.

The organo-alkali metal compounds used in the process of the invention is preferably a lithium, sodium or potassium compound. The organo group is attached to the metal by a carbon-to-metal linkage and may be an acyclic or cyclic hydrocarbon or hetero group which may be saturated or may be unsaturated and contain one or more olefinic or acetylenic linkages. The hydrocarbon or hetero group may carry one or more substituent groups which are inert with respect to the alkali metal substituent, for example, hydrocarbon, nitro, etherified hydroxyl and trifluoromethyl groups.

Examples of organo-alkali metal compounds which may be used in the process of the invention are butyllithium, ethylsodium, alkali metal alkyne derivatives, phenyllithium, sodium benzyl, potassium benzyl, sodium triphenylmethyl, o-aminophenyllithium and p-nitrophenyllithium.

The organo-alkali metal may be obtained by any process known in the art for preparing these compounds. A convenient method is to react a monohalohydrocarbon, preferably the chloro- or bromo-derivative, with two molecular proportions of the alkali metal, preferably in finely divided state or in thin strips, in an indifferent solvent. Anhydrous ether or ligroin are suitable solvents for this purpose. The organo-alkali metal thereby produced may be used in the process of the invention without being isolated, though it is desirable to remove precipitated alkali metal halide and unchanged alkali metal, for example, by decanting the supernatant liquid, preferably under anhydrous conditions. When the organo-alkali metal is prepared by this method, the alkali metal occupies the position of the halogen substituent in the original halogen compound.

Aryllithium compounds may also be prepared by reacting an alkyllithium, e.g. a butyllithium or amyllithium, either with an aromatic hydrocarbon or with a substituted derivative thereof such as, for example, an aryl ether or a trifluoromethyl substituted benzene. When the organolithium compounds are prepared by this method, metalation occurs predominantly in the ortho position to the substituent group.

The organo-alkali metal compound is reacted in the process of the invention with a halide, ester or ester halide of boric acid. As the halide of boric acid is preferably used boron trichloride or boron trifluoride either as such, or in the form of their addition compounds with an ether, for example, with the ether used as the reaction medium. Alternatively, a tri-ester of boric acid is used. This ester may be derived from an alcohol or from a phenol. Advantageously it is derived from an aliphatic alcohol containing from 1 to 5 carbon atoms in the molecule, such as propyl or butyl alcohol. Boron trihalides in which one or two halogen atoms have been replaced by an ester group or groups respectively may also be used in the process of the invention.

The reaction between the organo-alkali metal and the halide, ester or halide ester of boric acid in the process of the invention is effected in the absence of a hydroxylic compound, preferably by mixing the reactants in

liquid phase in the presence of an indifferent solvent such as diethyl ether. The reaction mixture should be well cooled, preferably to below 0°C., in order that the reaction may proceed smoothly.

The halide, ester or ester halide of the organoboron acid obtained as the reaction product of the process of the invention may be isolated by any suitable method. For example, the reaction mixture may be decanted and/or filtered, under anhydrous conditions where necessary, to remove precipitated byproducts such as alkali metal halides. The solvent and volatile impurities can then be removed by distillation and the residue purified by distillation, if necessary under reduced pressure, or by recrystallisation from a suitable solvent.

Alternatively, and according to a modification of the process of the invention, the reaction product may be hydrolysed to the corresponding organoboric acid by reaction with water. Where an ester of boric acid has been used as a reactant in the process of the invention, hydrolysis is preferably effected with an aqueous solution of a mineral acid to neutralise the alkali formed. Suitably, the reaction mixture is agitated with a dilute aqueous mineral acid solution, the solvent layer containing the organoboric acid separated and the solvent and any low boiling impurities such as alcohols removed by distillation. The residual organoboric acid may be purified by converting it into a salt and extracting the aqueous solution of the salt with a solvent, followed by acidification to liberate the purified organoboric acid. The organoboric acid may be recrystallised from benzene, aqueous alcohol or other suitable solvent. Owing to the readiness with which organoboric acids lose water to form anhydrides, it is preferable to use an aqueous organic solvent for recrystallisation.

The organoboron compounds produced by the process of the invention are chiefly mono-organoboron compounds. Small quantities of diorganoboron compounds are sometimes formed simultaneously and may be separated from the mono-organo compounds by fractional distillation, crystallisation or other suitable means. In some cases, it is possible to convert the diorganoboron compound into the mono-organoboron compound. Thus, diphenylboronic acid may be converted into phenylboronic acid by treatment with a halogen such as chlorine or bromine in presence of water, or with hydrogen peroxide.

The following examples illustrate the process of the invention, the parts by weight (p.b.w.) bearing the same relation to the parts by volume (p.b.v.) as the kilogram bears the litre.

EXAMPLE I

A solution of phenyllithium was prepared from bromobenzene (78.5 p.b.w.; 0.5 mol.) and lithium strips (8.6 p.b.w.; 1.25 atoms) in dry ether (375 p.b.v.) under an atmosphere of nitrogen. The solution was decanted from excess lithium and added dropwise with stirring to a solution of tri-n-butyl borate (116 p.b.w.; 0.5 mol.) in dry ether (200 p.b.v.), the reaction temperature being maintained at between −60°C. and −65°C. by cooling in a mixture of isopropyl alcohol and solid carbon dioxide. The reaction was allowed to warm to room temperature by standing overnight. The resulting solution was hydrolysed, by adding it dropwise to aqueous sulphuric acid (300 p.b.v.) containing 10 per cent by weight of H_2SO_4, which was stirred vigorously and cooled in an ice/salt bath.

The ether layer was separated and combined with the ether extracts obtained by extracting the aqueous layer twice using 100 p.b.v. of ether each time. The ether was removed by distillation, leaving a butanol solution which was made alkaline by adding potassium hydroxide (65 p.b.w.) in water (350 p.b.v.). The butanol was removed by steam distillation under a pressure of 28 millimetres of mercury and the aqueous solution was filtered from a gummy residue (2.5 p.b.w.) and acidified with aqueous sulphuric acid containing 10% by weight of H_2SO_4. The acid solution was heated to boiling, filtered hot and the residue extracted with boiling water (2×10 p.b.v.).

The filtrates were combined and cooled and the precipitated solid was collected and crystallised from a mixture of benzene (150 p.b.v.) and light petroleum (b.p. 40—60°C.; 50 p.b.v.) as a white powder (26.4 p.b.w.; 0.22 mol.; 43% yield) m.p. 215—216°C. (with oil bath preheated to 200°C.). This was phenylboronic acid.

EXAMPLE II

A solution of phenyllithium prepared from bromobenzene (314 p.b.w.; 2.0 mol.) and lithium (30.8 p.b.w.; 4.4 atoms) in dry ether (1400 p.b.v.) was decanted from excess lithium and added dropwise to a stirred solution of trimethyl borate (208 p.b.w.; 2.0 mol.) in dry ether (400 p.b.v.), the reaction temperature being maintained below −65°C. by cooling in a mixture of isopropyl alcohol and carbon dioxide. The clear solution was allowed to warm to room temperature overnight. It was then added slowly to aqueous sulphuric acid (1200 p.b.v.) containing 10 per cent by weight of H_2SO_4, with stirring and cooling in ice.

The ethereal layer was separated and the aqueous layer was extracted three times with ether, using 200 p.b.v. each time. The combined ether solutions were distilled to dryness from a boiling water bath and the off-white residue was crystallised from water and then from a mixture of equal parts by volume of benzene and light petroleum (b.p. 40—60°C.) giving colourless needles (20.5 p.b.w.; 0.17 mol.; 8.5% yield), m.p. and mixed m.p. 214—216°C.

The mother liquor was distilled to remove

the solvent, a black oily residue being obtained. (This residue [86.6 p.b.w.] was distilled under reduced pressure and gave an initial fraction consisting of water (about 25 p.b.w.) and a fraction which distilled at 88°C. under a pressure of 1.0 millimetres of mercury and was proved to be diphenyl).

The distillation residue was dissolved in aqueous ethanol solution containing 50 per cent by volume of ethanol and a solution of monoethanolamine (15 p.b.v.) in 15 p.b.v. of the aqueous ethanol solution was added. The mixture, from which a precipitate began to separate, was stirred at room temperature for 30 minutes, cooled in ice and filtered. The residue was dissolved in benzene, reprecipitated by adding light petroleum (b.p. 70°—95°C.) and finally crystallised from aqueous ethanol containing 30 per cent by volume of ethanol. The product was dried at 60°C. under 15 millimetres pressure of mercury for 2 hours, giving 2-aminoethyl diphenylborinate (6.3 p.b.w.) as off-white platelets, m.p. 189° C. Analysis, found N, 6.3%: calculated for $C_{14}H_{16}ONB$, N, 6.2%.

EXAMPLE III

Sodium phenyl was prepared as described by Gilman and Jones (J.A.C.S., 1940, 62, 1514) from chlorobenzene (50.6 p.b.w., 0.45 mol.) and sodium (23 p.b.w.; 1.0 atom) in toluene (300 p.b.v.). The resulting mixture was stirred and cooled to −30°C. during the dropwise addition of a slurry of methyl borate (52 p.b.w.; 0.5 mol.) in benzene (250 p.b.v.) also cooled to −30°C. The mixture was stirred and allowed to warm to room temperature. After 9 hours, ethanol (250 p.b.v.) was added, followed by water (500 p.b.v.). The aqueous layer was separated and stripped under reduced pressure until the volume was about 300 p.b.v. The solution was made up to 500 p.b.v. with distilled water and acidified (to Congo red indicator) with concentrated hydrochloric acid. The mixture was heated to boiling and filtered from a dark brown oil. Extraction of the cooled filtrate 5 times with ether (50 p.b.v. each time) followed by evaporation of the combined extracts gave a light brown residue. This was crystallized from water (100 p.b.v.) using decolourising charcoal.

Phenylboronic acid (5.5 p.b.w. 10% yield), was obtained, m.p. 215—216°C., when immersed in the bath preheated to 214°C.

The organo boron compounds produced by the process of the invention have use as intermediates and lubricant additives. In particular, the organo boron acids and their salts and esters are active in controlling the growth of plants, particularly of dicotyledonous plants and compositions containing them are featured in copending application No.

H. I. DOWNES,
Agent for the Applicants,
St. Helen's Court, Great St. Helen's,
London, E.C.3.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press.—1959.
Published by The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.